MODULE 2

A. SYMPATHETIC AUTONOMIC NERVOUS SYSTEM (SANS):

1. **Describe how the adrenergic neurotransmitter is synthesized, stored and released.**
    - **Synthesis of norepinephrine:** Tyrosine is transported by a carrier into the adrenergic neuron, where it is hydroxylated to dihydroxyphenylalanine (DOPA) by tyrosine hydroxylase. This is the rate-limiting step in the formation of norepinephrine. DOPA is then decarboxylated by the enzyme aromatic I-amino acid decarboxylase to form dopamine in the presynaptic neuron.
    - **Storage of norepinephrine in vesicles**: Dopamine is then transported into synaptic vesicles by an amine transporter system. This carrier system is blocked by reserpine. Dopamine is next hydroxylated to form norepinephrine by the enzyme dopamine β-hydroxylase.
    - **Release of norepinephrine:** An action potential arriving at the nerve junction triggers an influx of calcium ions from the extracellular fluid into the cytoplasm of the neuron. The increase in calcium causes synaptic vesicles to fuse with the cell membrane and to undergo exocytosis to expel their contents into the synapse. Drugs such as guanethidine block this release.

B. PARASYMPATHETIC AUTONOMIC NERVOUS SYSTEM (PANS):

1. **Describe how the cholinergic neurotransmitter is synthesized, stored and released.**
    - **Synthesis of acetylcholine:** Choline is transported from the extracellular fluid into the cytoplasm of the cholinergic neuron by an energy-dependent carrier system that cotransports sodium and can be inhibited by the drug hemicholinium. The uptake of choline is the rate-limiting step in ACh synthesis. Choline acetyltransferase catalyzes the reaction of choline with acetyl coenzyme A (CoA) to form ACh (an ester) in the cytosol.
    - **Storage of acetylcholine in vesicles:** ACh is packaged and stored into presynaptic vesicles by an active transport process coupled to the efflux of protons. The mature vesicle contains not only ACh but also adenosine triphosphate and proteoglycan. Cotransmission from autonomic neurons is the rule rather than the exception. This means that most synaptic vesicles contain the primary neurotransmitter (here, ACh) as well as a cotransmitter that increases or decreases the effect of the primary neurotransmitter.
    - **Release of acetylcholine**: When an action potential propagated by voltage-sensitive sodium channels arrives at a nerve ending, voltage-sensitive calcium channels on the presynaptic membrane open, causing an increase in the concentration of intracellular calcium. Elevated calcium levels promote the fusion of synaptic vesicles with the cell membrane and the release of their contents into the synaptic space. This release can be blocked by botulinum toxin. In contrast, the toxin in black widow spider

venom causes all the ACh stored in synaptic vesicles to empty into the synaptic gap.

2. **Describe the mechanism of action of the directly-acting and indirectly acting cholinergic drugs.**
   Direct-acting cholinomimetic agents bind to and activate muscarinic or nicotinic receptors. Indirect-acting agents produce their primary effects by inhibiting acetylcholinesterase, which hydrolyzes acetylcholine to choline and acetic acid. By inhibiting acetylcholinesterase, the indirect-acting drugs increase the endogenous acetylcholine concentration in synaptic clefts and neuroeffector junctions.

References:

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